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EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,678	BERGER ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 11-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date ~~3/21/2008~~.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-21 are currently pending. This is the first Office Action on the merits of the claims.

Election/Restrictions

2. Applicant's election with traverse of Group I, drawn to a homogenously reacetylated chitosan as recited in claims 10 and 18 in the reply filed on 12/15/2008 is acknowledged.

3. Applicant traverses on the grounds that there is no showing of a serious search burden in the Requirement for Restriction. As provided in 37 CFR 1.475(a), a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in a national stage application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Search burden is not a factor in determining lack of unity in a national stage application.

4. Applicant also traverses on the grounds that *Domard et al* do not disclose a homogenously reacetylated chitosan that meets the limitations of claim 10. As discussed below in more detail, *Domard et al* teaches chitosan (obtained from squid

endoskeletons, purified by dissolving, filtering, precipitating, washing and freeze-drying) (Paragraph 0033) which was re-acetylated with acetic anhydride in a hydro-alcoholic medium to obtain a degree of chitosan acetylation of 50% (Paragraph 0040). Furthemore, it does not involve an inventive step to homogenously reacetylate chitosan the chitosan taught by *Domard et al* as recited by instant claim 10. And although *Domard et al* do not disclose the molecular weight of the taught chitosan, "[w]here... the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433, 562 F2d 1252 (CCPA 1977). See also *In re Fitzgerald* 205 USPQ 594, 597, 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on." In the instant case, the chitosan taught by *Domard et al* is substantially similar to the instantly claimed chitosan and is produced by a substantially similar process. Accordingly, absent evidence to the contrary, it is asserted that the chitosan taught by *Domard et al* would have a molecular weight of not smaller than 200 kDa.

5. The requirement is still deemed proper and is therefore made FINAL.

6. Claims 1-9, 11-17 and 19-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Furthermore, newly amended claim 18 is directed to an invention that is independent or distinct from the elected invention. Specifically, in the

reply filed on 12/15/2008 Applicant elected Group I, drawn to a homogenously reacetylated chitosan. Newly amended claim 18 recites a method of making a phosphate-free, transparent, pseudo-thermosetting chitosan which falls within the non-elected Group V. Accordingly, claim 18 is also withdrawn from further consideration. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/15/2008.

Claim Rejections - 35 USC §103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claim 10 rejected under 35 U.S.C. 103(a) as obvious over *Domard et al* (WO 2002/078760) for which U.S. Patent No. 2004/0171151 is being used as the English**

language equivalent, as evidenced by *Industrial Research Ltd Catalog* (accessed online January 14, 2009) and *Granja et al* (Key Engineering Materials Vols, 254-256, 2004), and in view of *Varum et al* (WO 2003/011912), *Baumann et al* (Carbohydrate Res 1:43-57, 2001) and *Nettles et al* (Tissue Engineering 8:1009-1016, 2002).

9. Instant claim 10 is drawn to a homogenously reacetylated chitosan having a molecular weight of not smaller than 200 kDa and a deacetylation degree of 30-60% obtained by the process as claimed in claim 7 for use in the preparation of pseudo-thermosetting neutralized chitosan composition as recited.

10. *Domard et al* teaches chitosan (obtained from squid endoskeletons, purified by dissolving, filtering, precipitating, washing and freeze-drying) (Paragraph 0033) which is re-acetylated with acetic anhydride in a hydro-alcoholic medium to obtain a degree of chitosan acetylation of 50% (Paragraph 0040).

11. However, *Domard et al* do not teach that the chitosan is **homogenously** reacetylated as recited by instant claim 10. Yet, as disclosed by *Varum et al*, chitosans are generally prepared from chitin by only two methods: either homogenous or heterogenous deacetylation procedures (Page 4, Paragraph 2). Thus, under the circumstances (there being only two general procedures by which chitosan is reacetylated), one or ordinary skill would have at once envisaged reacetylating chitosan under homogenous conditions based on the generic disclosure of *Domard et al*. Additionally, as stated by Applicant, "in addition to the proportion of acetylated and deacetylated monomers of chitosan represented by its degree of deacetylation, the

homogenous distribution mode of these monomers is an essential criteria to get transparent and phosphate-free hydrogels" (Instant Specification Page 8, Lines 16-19). Notably, *Domard et al* specifically teach the formation of hydrogels from the re-acetylated chitosan without the addition of phosphate (Paragraphs 0042-0043). Accordingly, *Domard et al* teach the formation of phosphate-free hydrogels. Thus, it is asserted that the reacetylated chitosan taught by *Domard et al* must, by necessity, be homogenously reacetylated since homogenous reacetylation is an essential criterion to the formation of phosphate-free hydrogels. See *In re Fitzgerald* 205 USPQ 594, 597, 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on." Furthermore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to reacetylate the chitosan specifically using homogenous conditions as evidenced by *Baumann et al* which explicitly state that "reactions are to be carried out in homogeneous media, resulting in a statistical distribution of functional groups along the polymer chain. In contrast, heterogeneous reactions are known to result in block structures that cause solubility problems" (Page 44, Column 2). Thus, the skilled artisan would have been motivated to reacetylate the chitosan under homogeneous conditions in an effort to avoid solubility problems associated with heterogeneous reacetylation of chitosan.

12. *Domard et al* also do not disclose the molecular weight of the taught chitosan. However, as evidenced by the Industrial Research Ltd Catalog for Squid pen derived chitin and chitosan, "Squid pens contain β-chitin... therefore, squid pen derived β-chitin

is expected to have a higher molecular weight than crab or shrimp derived chitin. The chitosan preparted by deacetylating squid chitin is also expected to have a higher molecular weight than chitosan derived from other sources" (available online at http://www.irl.cri.nz/productsandservices/products-fine-chemicals/Squidpenderivedchitinandchitosan.aspx).

13. Furthermore, as evidenced by *Granja et al* (who teach injectable chitosa-hydroxyapatite microspheres for the promotion of localized bone regeneration (Abstract)) squid chitosan presented a viscosity average molecular weight of 2480 kDa (Page 573). Accordingly, although *Domard et al* do not explicitly disclose the molecular weight of the homogenously reacetylated chitosan, it is asserted that the homogenously reacetylated chitosan taught would have a molecular weight of not smaller than 200 kDa as recited by instant claim 10. "Where... the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433, 562 F2d 1252 (CCPA 1977). See also *In re Fitzgerald* 205 USPQ 594, 597, 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on." In the instant case, the chitosan taught by *Domard et al* is substantially similar to the instantly claimed chitosan and is produced by a substantially similar process. Accordingly, absent evidence to the contrary, it is asserted that the

chitosan taught by *Domard et al* would have a molecular weight of not smaller than 200 kDa.

14. Alternatively, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to provide chitosan having a molecular weight of not smaller than 200 kDa. As stated by MPEP 2144.05:

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)

. In the instant case, the molecular weight of chitosan is clearly a result-effective variable. As disclosed by *Domard et al*, the invention concerns the preparation of cartilaginous neo-tissue that is capable of being grafted (Abstract). As taught by *Nettles et al*, "properties of porous chitosan matrices such as microstructure, crystallinity, and mechanical strength can be varied by altering chitosan concentration, freezing rate, and the molecular weight and percent deacetylation of the starting material... Thus there are many ways to control and optimize the physical characteristics of chitosan scaffolds" (Page 1010, Column 1). Thus, the skilled artisan would have been motivated to optimize the molecular weight of the chitosan to provide scaffolds useable in the invention taught by *Domard et al* having the most desirable properties. In view of the disclosure of *Nettles et al*, a person of

ordinary skill in the art would have reasonably predicted that altering the molecular weight of the chitosan would accomplish this.

15. As to the recitation that the chitosan is "obtained by the process as claimed in claim 7", Applicant is reminded that:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted)

(MPEP 2113). In the instant case, the claimed homogenously reacetylated chitosan is obvious from the homogenously reacetylated chitosan taught by *Domard et al* in view of *Baumann et al* as discussed above.

16. As to the recitation that the claimed chitosan is "for use in the preparation of a pseudo-thermosetting neutralized chitosan composition...", Applicant is reminded that use limitations within product claims do not carry patentable weight unless the recitation of the intended use of the claimed invention results in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art.

17. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, the chitosan taught by *Domard et al* would be capable of being used in the preparation of a pseudo-thermosetting neutralized chitosan

composition forming a phosphate-free transparent hydrogel at a temperature higher than 5°C as claimed. Specifically, *Domard et al* teach that the reacetylated chitosan is "then poured into a receptacle that provided a large free surface/volume ratio and was then placed in an oven at 45°C for the time required for the gel to set" (Paragraph 0042) and "[t]o obtain a hydrogel which was not soluble in water at pHs of the order of 6 or 7, the hydrogel obtained was neutralized by placing it for about one hour in a basic medium, for example 0.1 molar sodium hydroxide" (Paragraph 0043). Accordingly, *Domard et al* teach the formation of a phosphate-free hydrogel at a temperature higher than 5°C. Furthermore, it is asserted that, absent evidence to the contrary, the hydrogel would be transparent. "Where... the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product" *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433, 562 F2d 1252 (CCPA 1977). See also *In re Fitzgerald* 205 USPQ 594, 597, 619 F2d 67 (CCPA 1980): the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on." In the instant case, the reacetylated chitosan taught by *Domard et al* in view of *Baumann et al* is substantially similar to the instantly claimed chitosan and is produced by a substantially similar process; furthermore, the hydrogel is substantially similar and produced by substantially the same process. Accordingly, absent evidence to the contrary, it is asserted that the resulting hydrogel taught by *Domard et al* in viewo of *Baumann et al* would be transparent.

18. Thus, for all of the foregoing reasons, instant claim 10 is rejected as *prima facie* obvious.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

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